



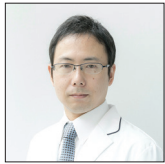
Case Report

¹¹C-methionine- and ¹⁸F-FDG-PET double-negative metastatic brain tumor from lung adenocarcinoma with paradoxical high ¹⁸F-FDG uptake: A case report

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ABSTRACT

Background: Imaging with ¹⁸F-fluorodeoxyglucose (FDG)-positron emission tomography (PET) and ¹¹C-methionine (MET)-PET can delineate primary and metastatic brain tumors. Lesion size affects the sensitivity of both scans and histopathological features can also influence FDG-PET, but the effects on MET-PET have not been elucidated.

Case Description: We report an unusual case of metastatic brain tumors without accumulation of FDG or MET, contrasting with high FDG uptake in the primary lung lesion. The brain lesions were identified as adenocarcinoma with a more mucus-rich background, contributing to the indistinct accumulation of both FDG and MET.

Conclusion: Histopathological characteristics can affect both MET and FDG accumulation, leading to findings contradicting those of the primary lesion.

Keywords: ¹¹C-methionine-PET, ¹⁸F-fluorodeoxyglucose-PET, Lung adenocarcinoma, Metastatic brain tumor, Mucus

INTRODUCTION

Tissue metabolism can be reflected by ¹⁸F-fluorodeoxyglucose (FDG)-positron emission tomography (PET) and ¹¹C-methionine (MET)-PET, making these imaging modalities useful for delineating and assessing both primary and metastatic brain tumors.^[1-4,6,8,9,11,12,14] Lesion size can significantly affect the sensitivity of detection,^[6-8,11] with FDG-PET able to delineate malignancies over 1.3 cm in diameter in the brain^[11] or over 2 cm in the lung,^[7] and MET-PET able to depict brain lesions larger than 0.5 mL with higher sensitivity without the influence of the metabolism of surrounding normal tissues.^[8] Some histopathological features are also known to impact the

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accumulation of FDG-PET,^[7] although the effects on MET-PET have not been clarified. In this report, we present a rare case of multiple metastatic brain tumors that both FDG- and MET-PET failed to depict, even though the lesions contained solid components of adequate size, along with a primary lung lesion showing paradoxical high uptake of FDG.

CASE DESCRIPTION

A 63-year-old man with the left deafness due to a small left acoustic neurinoma presented with a 1-month history of dizziness and gait disorder. Contrast-enhanced magnetic resonance imaging (MRI) demonstrated multiple tumors in the right cerebellar hemisphere, right cerebellar peduncle, and right parietal lobe [Figures 1a-c]. Computed tomography (CT) of the chest revealed a mass lesion in the inferior lobe of the left lung [Figure 1d]. Both FDG- and MET-PET demonstrated no significant accumulation in the brain lesions [Figures 2a and b], while FDG-PET showed high uptake in the lung lesion [Figure 2c]. Transbronchial lung biopsy revealed moderately differentiated adenocarcinoma. No gene mutation for molecular-targeted therapy was identified as of this point [Figures 3a and b].

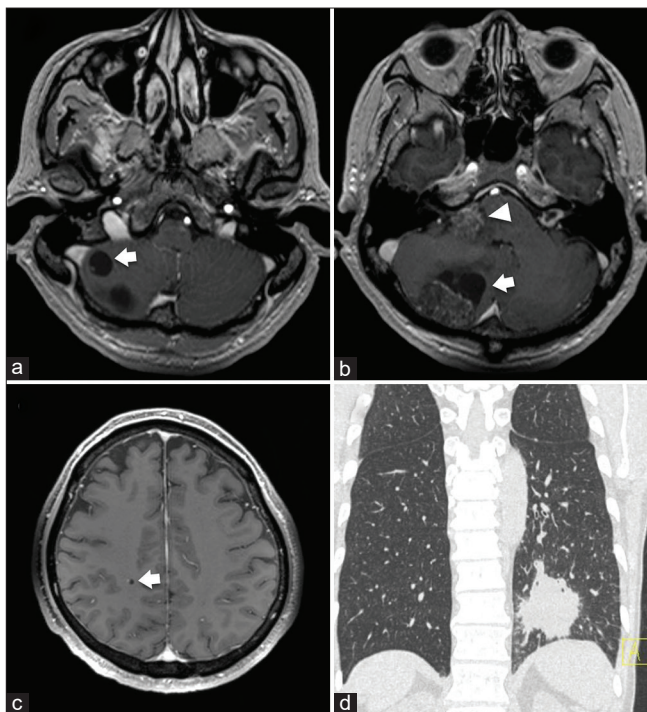


Figure 1: (a-c) Gadolinium-enhanced magnetic resonance imaging of the brain at the initial visit. Two enhanced lesions are apparent in the right cerebellar hemisphere (31×19 -mm solid component with 24×14 -mm cystic part; 10×10 -mm cystic tumor, arrows), one in the right cerebellar peduncle (22×18 mm, arrowhead) (a and b), and one in the right parietal lobe (5×4 mm, arrow) (c). (d) Computed tomography of the lung at the initial visit. A mass lesion is seen in the inferior lobe of the left lung.

The treatment for the brain lesions was planned before systemic chemotherapy. To preserve remaining right hearing, stereotactic radiotherapy or fractionated stereotactic radiosurgery (SRS), which would reduce the adverse effects on the acoustic nerve, was considered more suitable than open surgery for the lesion in the right cerebellar peduncle. However, resection was preferable for the lesion in the right cerebellar hemisphere given its larger size (>3 cm) and the need for histopathological diagnosis since the negative findings from both FDG- and MET-PET contradicted the high FDG uptake of the lung lesion.

Under general anesthesia, the lesions in the right cerebellar hemisphere were completely resected through a right suboccipital craniotomy in a prone position, with the lesion in the right cerebellar peduncle left untouched. The resected specimens were submitted for histopathological examination.

The postoperative course was uneventful and symptoms ameliorated. Histopathological examination revealed that the cerebellar lesions represented adenocarcinoma consistent with the lung lesion. However, more mucous-rich components were observed in the cerebellar lesions [Figure 3c]. Fractionated SRS was administered for the remaining lesions (27.5 Gy in five fractions to the lesion in the right cerebellar peduncle and 35 Gy in five fractions to the lesion in the right parietal lobe) from 1 month after surgery. Shrinkage of the remaining lesions was attained by 3 months [Figures 4a and b] and no recurrence has been observed as of 4 years and 5 months after the completion of fractionated SRS, although additional SRS has been required for new metastatic lesions [Figure 4c].

DISCUSSION

FDG-PET is well known to be useful for delineating malignant tumors by assessing metabolic activity.^[3,4,6,7,9,11,14] However, the high glucose utilization of the normal brain frequently complicates the identification of brain tumors.^[3,6,8,11,15] On the other hand, due to the low uptake of amino acids in the brain, the contrast between tumors and normal brain is generally better visualized with amino acid scanning.^[8,12,15] Although the degree of FDG uptake does not always reflect the grade or progression of primary brain tumors,^[4,14] MET-PET is more efficient in delineating gliomas and in differentiating recurrence from radiation necrosis.^[1,2,9,12,15]

The negative rate of FDG-PET has been reported as 32–39% in metastatic brain tumors detectable on CT or MRI.^[3,6,11] Rohren *et al.* showed that size represented a significant factor in the lesion conspicuity of metastatic brain lesions and the average diameter not detected on PET was 0.7 cm (range, 0.2–1.3 cm),^[11] while Matsuo *et al.* showed precise delineation of tumors with volumes >0.5 mL by MET-PET.^[8] In our case, none of the four brain lesions were depicted on FDG- or

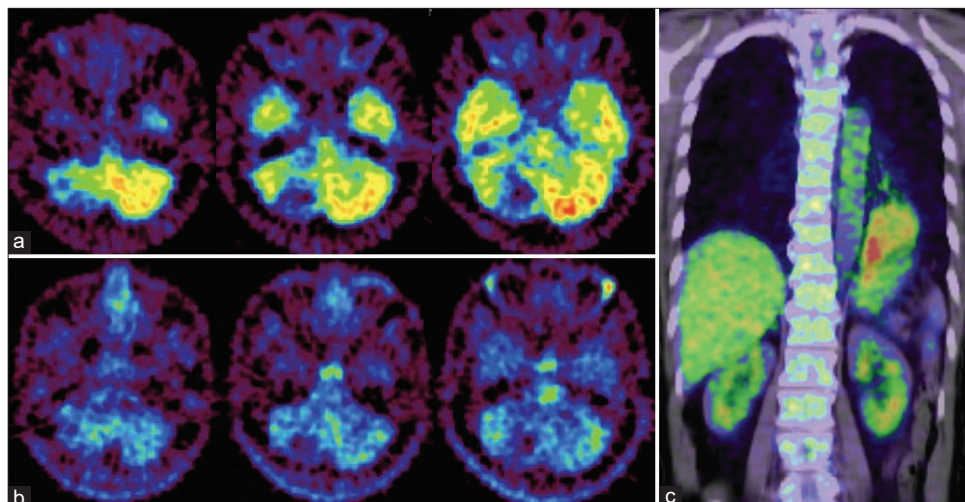


Figure 2: Positron emission tomography (PET) of the brain and lung. (a and b) Images of brain PETs. Neither ^{18}F -fluorodeoxyglucose (FDG)-PET (a) nor ^{11}C -methionine-PET (b) shows significant uptake in the areas identified on gadolinium-enhanced magnetic resonance imaging [Figure 1] compared to surrounding normal brain tissue. (c) Image of lung FDG-PET. A high-uptake lesion is seen in the inferior lobe of the left lung.

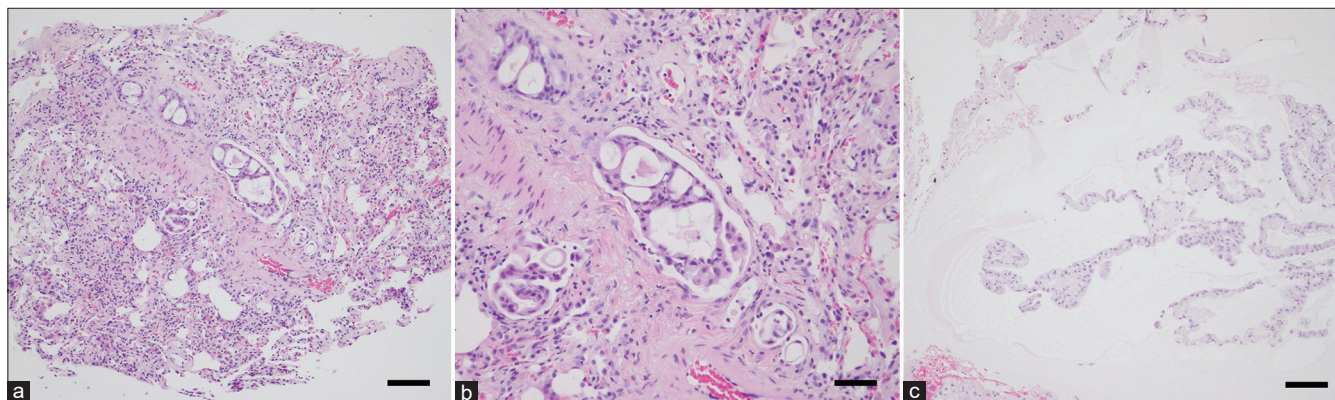


Figure 3: Histopathological examinations of the lung and cerebellar lesions. (a and b) Acinar and cribriform patterns of tumor cells with increased chromatin and some mucin are invading the lung, showing moderately differentiated adenocarcinoma. Bar = 100 μm (a), Bar = 50 μm (b). (c) Columnar mucinous cells containing moderate cytological atypia and clear cytoplasm are forming a lepidic pattern in a mucin-rich background. The diagnosis is corresponding to the metastasis of lung adenocarcinoma. Bar = 100 μm .

MET-PET, even though at least two lesions contained solid components sufficiently larger than 0.5 mL [Figure 1b].

The histological class of “colloid/mucinous/lepidic” in the international multidisciplinary classification of lung adenocarcinoma^[13] has also been reported as the only relevant factor for negative FDG-PET results in the primary lung cancers, although details of the metabolic mechanisms involved have yet to be ascertained.^[7] The effect of histological characteristics on MET-PET has not yet been investigated. In our case, the brain lesions represented moderately differentiated adenocarcinoma with a mucus-abundant background [Figure 3c]. Tumor cells were distributed sparsely in the mucus of the metastatic lesions, which seems likely to have contributed to the indistinct accumulation of FDG and MET.

Regarding the discrepancies between metastatic and primary lesions in PET findings, Lee *et al.* demonstrated that 32.7% of brain lesions depicted on MRI were not clearly detectable on FDG-PET, despite high FDG uptake in all primary lung lesions.^[6] Lesion size was not significantly related to the FDG-negative findings and small cell lung cancer was more frequently associated with hypometabolic brain lesions than non-small-cell lung cancer (NSCLC), including adenocarcinoma. Glucose metabolism is central to the accumulation of FDG and could differ in the context of brain metastasis from that in the primary lesion.^[5] In our case, the brain lesions represented NSCLC, consistent with the primary lung lesion. However, the brain lesions showed increased mucus proliferation compared to the primary

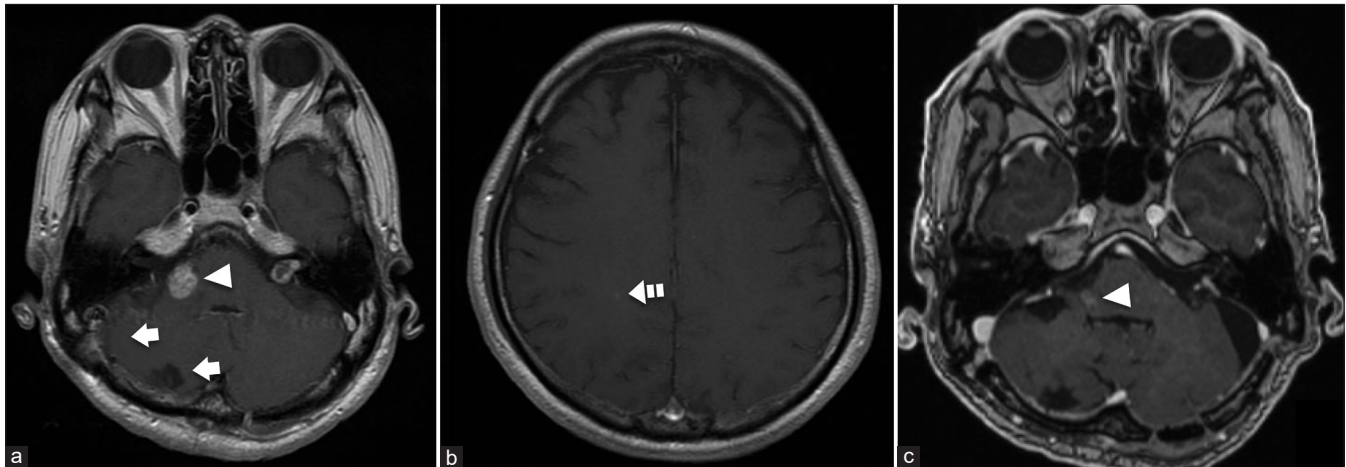


Figure 4: Gadolinium-enhanced magnetic resonance imaging of the brain after treatment. (a and b) The two cerebellar lesions are resected, and fractionated stereotactic radiosurgery (SRS) is administered to the lesions in the right cerebellar peduncle and right parietal lobe. No evidence of recurrence is demonstrated in the right cerebellar hemisphere (arrows). The lesion in the right cerebellar peduncle shows slight shrinkage 3 months after the completion of SRS (arrowhead) (a). The lesion in the right parietal lobe is stable (dashed arrow) (b). (c) The lesion in the right cerebellar peduncle shows marked shrinkage 4 years and 5 months after the completion of SRS (arrowhead) with no recurrence of the other lesions.

lesion, apparently causing the discrepancies in PET findings. The transition of histological characteristics might be attributable to clonal heterogeneity between the primary and metastatic lesions.^[10]

CONCLUSION

In addition to lesion size, histopathological features of metastatic brain tumors could be associated with negative findings on MET-PET as well as FDG-PET, which can contradict findings from the primary lesion. Proper assessment of results from PET studies is important when deciding on treatment strategies for metastatic brain tumors.

Declaration of patient consent

Institutional Review Board (IRB) permission obtained for the study.

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Conflicts of interest

There are no conflicts of interest.

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